IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No	:	10/582,982 Confirmation No.: 1560
Applicants	:	Robert C. Shipman and David K. H. Lee
Filed	:	June 15, 2006
Title	:	Materials and Methods for Analysis of ATP-Binding Cassette Transporter Gene Expression
TC./A.U.	:	1634
Examiner	:	POHNERT, Steven C.
Docket No.	:	13516-4
Customer No.	:	001059

Honorable Commissioner for Patents
P. O. Box 1450
Alexandria, Virginia 22313–1450

Dear Sir:

DECLARATION UNDER 37 CFR §1.132

I, Robert C. Shipman, a citizen of Canada, and resident of Mississauga, Ontario, Canada, declare that the following facts are within my knowledge and are true.

1. I reside at 130 Vista Boulevard, Mississauga, Ontario, Canada L5M 1V9.

2. I currently am the Director of Genomics at NoAb Biodiscoveries Inc., 2820 Argentia Road, Unit 8, Mississauga, Ontario L5N 8G4.

3. I have been working in the area of molecular biology since 1980. My *curriculum vitae* is attached to this Declaration as Exhibit A.

4. I am an inventor of the subject matter as claimed in U.S. Patent Application No. 10/582,982, filed June 15, 2006 (hereafter "the Application").

5. I have read and understood the disclosure and claims of the Application.

6. I have read and understood the Office Action that issued on the Application on August 7, 2008. The Examiner is of the view that claims 49, 50, and 78 are obvious under 35 USC § 103(a) over Denefle et al (WO02/46458) in view of Dean et al (J. Lipid Research, 2001, 42:1007-1017); Monahan et al (Wo02/071928); Schmitz (WO00/18912); GenBank AC069137.6; Boyd et al (WO01/62977); GenBank U63970.1; Wan et al (WO2002/74979); Kruh et al (WO99/49735); GenBank Z31010.1; and Ota et al (EP1074617A2).

7. I have read and understood the claims that are attached to this Declaration as Exhibit B that were filed on October 28, 2008 in response to the Office Action dated August 7, 2008. My comments below are based on the amended claims in Exhibit B (hereinafter "the amended claims").

8. The amended claims are limited to a combination of nucleic acid sequences that each specifically hybridize to one ABC transporter gene.

9. Denefle teaches nucleic acids corresponding to various exons of ABC transporter genes ABCA5, ABCA6, ABCA9, and ABCA10 genes as well as cDNAs encoding the novel full length of ABCA5, ABCA6, ABCA9, and ABCA10 proteins. Denefle also mentions that the invention described therein includes nucleotide probes and primers hybridizing with a nucleic acid sequence located in the region of any one of ABCA5, ABCA6, ABCA9, and ABCA10 nucleic acids (genomic DNA, messenger RNA, cDNA), and that these probes may be immobilized on a support.

10. Dean is a journal article that reviews the current state of knowledge on all

human ABC genes in inherited disease and drug resistance.

12. Monahan, Schmitz, GenBank AC069137.6, Boyd, GenBank U63970.1, Wan, Kruh, GenBank Z31010.1 and Ota describes the full length gene sequence for ABC transporter B1, B4, B11, C1, C2, C3, C4 and C5 (both in Kruh), D1 and G2, respectively.

13. None of the cited documents teach or suggest the any one of the nucleic acid sequences consisting of SEQ ID NO: 12, 15, 21, 22, 23, 24, 25, 26 35 or 44 as claimed in claim 49 of the amended claims. Further, none of the cited documents teach or suggest an array comprising a substrate and, immobilized thereon, in distinct spots, at least 10 nucleic probes consisting of SEQ ID NOS: 12, 15, 21, 22, 23, 24, 25, 26 35 and 44 as claimed in claim 78 of the amended claims.

14. The Examiner contends that the claimed SEQ ID NOS are obvious over the cited art, absent secondary considerations, because "[t]he substitution or deletion of the sequences taught [in the cited art] in the arrays taught by Denefle would produce a microarray with probes equivalent to the recited SEQ ID NO by replacing or adding known ABC transporter gene sequences for another. The artisan would have a reasonable expectation of success as methods of synthesizing nucleic acids and making arrays as well as the sequences of ABC transporter genes were known at the time of the invention".

15. I agree that methods of synthesizing nucleic acids and making arrays were known in the art at the time we made this invention, however, I disagree with the Examiner's submission that "there are many internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet". To my knowledge, no such programs exist. While the prior art may teach parameters and objectives involved in the selection of pcr primers and provide software for the selection of relatively short

oligonucleotides such as *pcr primers*, the prior art does not teach the necessary information that would allow a person skilled in the art to identify probe sequences such as the specific nucleic acid sequences found in the Application.

16. To verify that the known pcr primer selection programs do not provide the sequences claimed in the amended claims, we have accessed the widely used, and freely available, PCR primer design program called Primer3 (http://frodo.wi.mit.edu) and asked it to provide sets of primers and PCR products for each of the ABC transporter genes, B1, B4, B11, C1, C2, C3, C4, C5, D1 and G2. Using the default parameters, Primer3 does not return any of the PCR primer sequences or PCR products reported and claimed in the Application. Primer3 preferentially returns short (<300 bp) PCR products since this is the most efficient size for PCR/Taq polymerase processing rates and reduced mis-incorporation of base pairs. We then changed the default Primer3 parameters to obtain PCR product sizes in the same range as those in the Application, and Primer3 still did not return the PCR primer sequences or PCR product sequences reported and claimed in the Application.

17. To verify that the PCR products identified using Primer3 are not equivalent to those taught in the application we ran BLAST searches for both the Primer3 PCR products (obtained using the non-default product size range) and the PCR products from the Application. Below is a table containing the results. As can be seen, the numbers were higher (i.e. better) for the sequences from the Application. The values shown for each gene represent the values from the highest quality match in the BLAST search record (first line, highest identity match to the entire query sequence). The higher the number the better the match between the sequences and the better the chance that, under stringent hybridization conditions, the sequence will act as a probe for that sequence.

	BLAST Results for Sequences from the Application		BLAST Results for Sequences from Primer3	
ABCT Gene	Max Score	Total Score	Max Score	Total Score
B1	1420	1553	672	767
B4	1425	1618	724	724
B11	1328	1382	856	856
C1	1191	1405	616	616
C2	1462	1462	563	563
C3	1303	1303	688	688
C4	1433	1433	883	883
C5	1166	1166	836	836
D1	881	881	848	848
G2	1126	1126	884	884

18. The results shown in the Table above, show that freely available web-based PCR primer design software [ie. Primer3] does not generate probes or sequences that are equivalent to the ones that are claimed in the amended claims. Therefore the claimed sequences are in no way predictable based on the teachings of the cited art.

19. In further support of the unpredictability of the sequences that are claimed in the amended claims, it should also be noted that PCR primers that have been designed *in silico* to produce a single PCR product will frequently generate multiple PCR products in practice. In arriving at the present invention, almost every computer-generated PCR primer set had to be modified or redesigned using my experience and knowledge, at least once to obtain a sequence that worked in practice.

20. Still further, in arriving at the present invention, there were many examples of PCR primers that produced a single PCR product that, when cloned and sequenced, was not the gene it was designed to amplify. Again, using my experience and knowledge, the primer sequences had to be modified or

redesigned. There was also an occurrence where the PCR primers produced a single product that, when cloned, was lethal to the cells being transfected and transformed.

21. The examples described in Items 19 and 20 underline the assertion that there is no way to predict that any given PCR product will be a functional probe for a chosen nucleic acid sequence. In all cases, sequences selected using computer programs need to be verified and validated and in almost all cases, the experience, knowledge and skill of a senior scientist is required to obtain a sequence that, when reduced to practice, provides the desired probe product and performance in gene expression analyses.

22. In summary, I believe that we are entitled to claim the combination of nucleic acid sequences that each specifically hybridize to one ABC transporter gene that is found in the amended claims because these sequences are in no way predictable based on the teachings of the cited art and the knowledge of a person skilled in the art. This is because, using the teachings of the cited art, a person skilled in the art would not obtain products that would function as probes for the ABC transporter genes and therefore would not obtain products that are equivalent with the claimed sequences.

23. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statement and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the Application or patent resulting therefrom.

Jan. 19. 2009
Date

Robert C. Shipman, Ph.D.

EXHIBIT A

Curriculum Vitae

I. Degrees/Theses:

B.Sc. (1980) The University of British Columbia
A Common Leukemia-Associated Antigen in Human Acute Myelogenous Leukemia.

M.Sc. (1982) The University of British Columbia
Isolation of a Cell Surface Antigen specific for Human Acute Myelogenous Leukemia Cells.

Ph.D. (1987) The University of British Columbia
Characterization of a Common Myelogenous Leukemia-Associated Antigen (CAMAL) in Human Myelogenous Leukemia.

II. Previous Employment:

October 1987- July 1990
Project Leader, Inflammation and Cytokines Research Group,
Biotechnology K681.506, Pharma Research,
CIBA-GEIGY AG, Basel, Switzerland.

August 1990- July 1995
Lab Director and Project Leader, Molecular Oncology,
University Hospital Research Center (Zentrum fuer Lehre und Forschung),
KANTONSSPITAL BASEL, Basel, Switzerland.

September 1995- January 1996
Lab Director, Medical Genetics,
Division of Cellular and Molecular Biology,
ONTARIO CANCER INSTITUTE, Toronto, Ontario, Canada.

January 1996- August 1999
Project Manager-Molecular Pathology (p53/Brca1/Brca2),
Project Manager-Infectious Disease (Drug Resistant Tuberculosis),
Senior Scientist,
VISIBLE GENETICS INC., Toronto, Ontario, Canada.

June 2000- Present
Director- Genomics,
NOAB BIODISCOVERIES INC., Mississauga, Ontario, Canada

III. Professional societies:

1. American Association of Cancer Research (AACR)

2. American Association of Pharmaceutical Scientists (AAPS)

3. Collaborative Health Research Projects (CHRP) Grant Selection Committee Member 2003-2005
Collaborative Health Research Projects (CHRP) Grant Selection Committee Chair 2006

4. Canadian Institutes of Health Research (CIHR) Institute of Genetics Advisory Board Member 2004-2007

IV. Patents:

1. Method and Reagents for testing for mutations in the BRCA1 gene
(Issued June 11, 2002 - US6403303).

2. Method for single tube sequencing of nucleic acid polymers
(Issued July 4, 2000 – US6083699).

V. Invited presentations/seminars:

1. Allelic loss and alteration of tumour suppressor genes in human lung and bladder carcinoma. 10th Annual Meeting of the OAO/GTOR (Upper Rhine Oncology Association),
1994, Basel, Switzerland.

2. Alterations of putative tumour suppressor genes in human non-small cell lung carcinoma (NSCLC). 26th Annual Meeting of the USGEB/USSBE (Swiss Union of Biological Sciences), 1994, Bern, Switzerland.

3. Preferential allelic loss of the catalase gene (CAT) at 11p13 in human non-small cell lung cancer. Swiss Society for Oncology, 1994, Bern, Switzerland.

4. Preferential allelic loss of the CAT locus at chromosome 11p13 and the isolation of genes involved in the development of non-small cell lung cancer. C.R. Brupbacher Foundation 2nd Scientific Symposium: Genetic Predisposition to Cancer, 1995, Zurich, Switzerland.

5. Development of a stratified approach for the detection of gene mutations in genomic DNA of patient samples. Gene Mutational Analysis, Cambridge HealthTech Institute, September 30-October 1, 1996, Baltimore MD.

6. Analysis of putative tumour suppressor genes in human lung and bladder cancer. 5th

Annual Seminar on Molecular Pathology: DNA technology in the Clinical Laboratory, Beaumont Pathology Conferences, March 8-9, 1996, Royal Oak MI.

7. Complete p53 gene analysis using the OpenGene system: Mutation detection in genomic DNA from archival and fresh clinical specimens. Toronto Molecular Pathology/Molecular Diagnostics Group, Sunnybrook Health Sciences Centre, July 31, 1997, Toronto, Ontario.

8. Complete p53 gene analysis using the OpenGene system: Mutation detection in genomic DNA from archival and fresh clinical specimens. Association for Molecular Pathology Annual Meeting, November 12-15, 1997, San Diego CA.

9. Industrial applications of molecular biology. Genetics Technology post-diploma program, The Michener Institute for Applied Health Sciences, March 12, 1998, Toronto, Ontario.

10. Molecular applications in Biotechnology. Introduction to molecular DNA techniques, The Michener Institute for Applied Health Sciences, June 26, 1998, Toronto, Ontario.

11. Complete p53 gene analysis using the OpenGene system: Mutation detection in genomic DNA from archival and fresh clinical specimens. 3rd Annual New Cancer Strategies: P53, Cambridge Healthtech Institute, September 16-17, 1998, Washington DC.

12. Rapid detection of antibiotic resistance-associated mutations in 10 gene targets in Mycobacterium tuberculosis using the OpenGene system. Third Annual Conference on Microbial Genomes, The Institute for Genomic Research, January 29-February 1, 1999, Chantilly VA.

14. Industrial applications of molecular biology. Genetics Technology post-diploma program, The Michener Institute for Applied Health Sciences, March 10, 1999, Toronto, Ontario.

15. Complete p53 gene analysis using the OpenGene system: Mutation detection in genomic DNA from archival and fresh clinical specimens. 50th Annual Meeting of the Canadian Association of Pathologists, June19-22, 1999, Calgary, Alberta.

16. Molecular applications in Biotechnology. Introduction to molecular DNA techniques, The Michener Institute for Applied Health Sciences, June 25, 1999, Toronto, Ontario.

17. Rapid detection of antibiotic resistance-associated mutations in 12 gene targets in Mycobacterium tuberculosis using the OpenGene system. 20th Annual Congress of the European Society of Mycobacteriology, July 4-7, 1999, Lucerne, Switzerland.

VI. Publications:

1. A.Kh. Al-Rammahy, R. Shipman, A. Jackson and J.G. Levy (1980). Evidence for a common leukemia-associated antigen in human acute myelogenous leukemia. Cancer Immunol. and Immunother. 9: 181-185.

2. A.J. Malcolm, R. Shipman and J.G. Levy (1981). Detection of a tumour-associated antigen on the surface of human acute myelogenous leukemia cells. J. Immunol. 128: 2599-2603.

3. A.J. Malcolm, P.M. Logan, R. Shipman, R. Kurth and J.G. Levy (1983). Analysis of human myelogenous leukemia cells in the fluorescence-activated cell sorter using a tumour-specific antiserum. Blood 61: 858-866.

4. R. Shipman, A.J. Malcolm and J.G. Levy (1983). Partial characterization of a membrane antigen which exhibits specificity for cells of patients with acute myelogenous leukemia. Br. J. Cancer 47: 849-852.

5. A.J. Malcolm, R. Shipman, P.M. Logan and J.G. Levy (1984). A monoclonal antibody to myelogenous leukemia: isolation and characterization. Exp. Hematol. 12: 539-547.

6. R. Shipman and J.G. Levy (1988). Expression of a leukemia-associated antigen (CAMAL) in four myeloid leukemia cell lines. Leukemia Res. 12: 537-543.

7. J.K. Lazdins, T. Klimkait, K. Woods-Cook, M. Walker, E. Alteri, D. Cox, N. Cerletti, R. Shipman, G. Bilbe and G. McMaster (1991). HIV-1 lymphocytotropic restriction is overcome by TGF-□, an enhancer of viral expression in mononuclear phagocytes. J. Immunol. 147: 1201-1207.

8. J.K. Lazdins, T. Klimkait, E. Alteri, M. Walker, K. Woods-Cook, D. Cox, G. Bilbe, R. Shipman, N. Cerletti and G. McMaster (1991). TGF-□: upregulator of HIV replication in macrophages. Res. Virol. 142: 239-242.

9. G. Bilbe, J. Delabie, J. Bruggen, H. Richener, F.A.M. Asselbergs, N. Cerletti, C. Sorg, K. Odink, L. Tarcsay, W. Wiesendanger, C. DeWolf-Peeters and R. Shipman (1992). Restin, a new class of intermediate filament-associated protein highly expressed in the Reed-Sternberg cells of Hodgkin's disease. EMBO J. 11: 2103-2113.

10. J.Delabie, R. Shipman, J. Bruggen, B. De Strooper, F. Van Leuven, L.Tarscay, N. Cerletti, K. Odink, V. Diehl, G. Bilbe and C. De Wolf-Peeters (1992). Expression of the novel intermediate filament-associated protein "restin" in Hodgkin's disease and anaplastic large cell lymphoma.

Blood 80: 2891-2896.

11. P. Schraml, R. Shipman and C.U. Ludwig (1993). cDNA subtraction library construction using a magnet-assisted subtraction technique (MAST). Trends Genet. 9 (3): 70-71.

12. R. Shipman, P. Schraml, M. Colombi, G. Raefle and C.U. Ludwig (1993). Loss of heterozygosity on chromosome 11p13 in primary bladder carcinoma. Hum. Genet. 91: 455-458.

13. S.Park, M. Schalling, A. Bernard, S. Maheswaran, G.C. Shipley, D. Roberts, J. Fletcher,
R. Shipman, J. Rheinwald, G. Demetri, J. Griffin, M. Minden, D.E. Housman and D. Haber (1993). The Wilms tumor gene WT1 is expressed in mesoderm-derived tissues and mutated in mesothelioma.
Nature Genet. 4: 415-420.

14. C.U. Ludwig, M. Gencik and R. Shipman (1993). Multistep transformation in low grade lymphoproliferative diseases.
Annals Oncology 4: 825-830.

15. R. Shipman (1994). Applications of the polymerase chain reaction to tumour analysis and diagnosis. In: Klapdor, ed. Current Tumor Diagnosis: Applications, Clinical Relevance, Research, Trends.Cancer of the Lung- State and Trends in Diagnosis and Therapy.
Munich, W. Zuckerschwerdt Verlag GmbH, pp. 839-845.

16. R. Shipman and P. Schraml (1995). Reverse Transcription PCR (RT-PCR) from total RNA. In: PCR Applications Manual. Boehringer Mannheim GmbH. pp. 87-94.

17. R. Shipman and P. Schraml (1995). Analysis of p53 point mutations using PCR. In: PCR Applications Manual. Boehringer Mannheim GmbH. pp. 158-160.

18. R. Shipman and P. Schraml (1995). Detection of allelic loss in tumour tissue genomic DNA by amplified fragment length polymorphism PCR (AFLP-PCR) using variable number tandem repeat (VNTR) sequence primers or microsatellite sequence primers. In: PCR Applications Manual. Boehringer Mannheim GmbH. pp. 161-165.

19. P. Schraml, R. Shipman, M. Colombi and C.U. Ludwig (1994). Identification of genes differentially expressed in normal lung and non-small cell lung carcinoma tissue. Cancer Res. 54: 5236-5240.

20. A. Juretic, G.C. Spagnoli, H. Horig, R. Shipman, T. Kocher, F. Harder and M. Heberer (1995). Tyrosine kinase dependent and independent events induced by IL-2 stimulation: IL-2 mediated NO production required for the induction of LAK cell activity in rat splenocytes is tyrosine kinase dependent.

Immunology 85: 325-330.

21. P. Schraml, R. Shipman and C.U. Ludwig (1996). Screening cDNA Libraries: Isolating the 5' end of a cDNA from a lambda cDNA library with PCR. Focus (Life Technologies Inc.) 18 (2): 38-39.

22. R. Shipman, P. Schraml, M. Colombi, E. Schultheiss, G. Raefle, P. Dalquen and C.U. Ludwig (1996). Frequent p53 gene alterations (mutation, allelic loss, nuclear accumulation) in primary non-small cell lung cancer. Eur. J. Cancer 32A: 335-341.

23. R. Shipman, P. Schraml, H. Moch, M. Colombi, G. Sauter, M.J. Mihatsch and C.U. Ludwig (1997). p53 protein accumulation and p53 gene alterations (RFLP, VNTR and p53 gene mutations) in non-invasive versus invasive human transitional bladder cancer. Int. J. Oncology 10: 801-806.

24. R. Shipman, P. Schraml, M. Colombi and C.U. Ludwig (1998). Allelic deletion at chromosome 11p13 defines a tumour suppressor region between the catalase gene and D11S935 in human non-small cell lung carcinoma. Int. J. Oncology 12: 107-111.

25. R. Shipman and J. Dunn (1998). Fluorescence-based automated DNA sequencing. Biomedical Products 23 (5): 38-40.

26. M.E. Saunders, R. MacKenzie, R. Shipman, E. Fransen, R. Gilbert and R.C.K. Jordan (1999). Patterns of p53 gene mutations in head and neck cancer: Full-length gene sequencing and results of primary radiotherapy. Clin. Cancer Res. 5:2455-2463.

27. P.C.M. Larsson, B. Beheshti, H.A Sampson, M.A.S. Jewett and R. Shipman (2001). Allelic deletion fingerprinting of urine cell sediments in bladder cancer. Mol. Diagnosis 6:181-188.

28. P.C.M. Larsson, B. Beheshti, R. Shipman and M.A.S. Jewett (2001). Allelic deletion analysis of multiple bladder tumors. UroOncology 1:291-295.

VII. Abstracts presented at conferences:

1. R. Shipman and J.G. Levy (1981). Isolation and Partial Characterization of a Leukemia-Associated Antigen on the Surface of Human Acute Myelogenous Leukemia Cells. Proceedings of the International Symposium on the Cellular and Molecular Biology of Hematopoetic Stem Cell Differentiation. Ontario Cancer Institute and the National Cancer Institute. Honey Harbour, ON.

2. R. Shipman, A.J. Malcolm and J.G. Levy (1981). Detection and Isolation of a Leukemia-Associated Antigen on the Surface of Human Acute Myelogenous Leukemia Cells. Pacific Northwest Immunology Group Meeting. The Fred Hutchinson Cancer Institute. Friday Harbour, San Juan Island, WA..

3. R. Shipman, P.M. Logan, V. Lum and J.G. Levy (1984). Isolation of a Common Myelogenous Leukemia-Associated Antigen and its Detection in Human Myelogenous Leukemia Cells using Immunoperoxidase. ICN/UCLA Symposium on Molecular and Cellular Biology: Leukemia 1985. Keystone, Colorado, USA.

4. R. Shipman and J.G. Levy (1986). Characterization of a Common Myelogenous Leukemia-Associated Antigen (CAMAL) from Human Myelogenous Leukemia Cells. 6th International Congress of Immunology. Toronto, ON.

5. J. Lazdins, E. Alteri, M. Walker, K. Woods-Cook, Th. Klimkait, D. Cox, G.Bilbe, R. Shipman, N. Cerletti and G. McMaster (1990). Role of TGFb in HIV-1 replication in macrophages. Franco-German Cooperation on AIDS Research Symposium: Macrophages as Target Cells of HIV. Freiburg im Breisgau, Germany.

6. J. Lazdins, E. Alteri, M. Walker, K. Woods-Cook, D. Cox, G. Bilbe, R. Shipman, N. Cerletti and G. McMaster (1990). TGFb upregulation of HIV replication in macrophages. 27th Annual Meeting of the Society for Leukocyte Biology. Heraklion-Crete, Greece.

7. R. Shipman, P. Schraml, G. Raefle and C.U. Ludwig (1991). Deletions of putative tumour suppressor genes in human non-small cell lung carcinoma. AACR Special Conference: Negative controls on cell growth and their breakdown during the pathogenesis of cancer. Chatham, MA.

8. T. O'Reilly, S. Kunz, R. Shipman, L. Tarcsay and G. Bilbe (1992). In Vivo induction of cytokine mRNA following administration of liposomal MTP-PE (CGP 19835A) to mice.
32nd ICAAC, American Society for Microbiology. Anaheim, CA.

9. R. Shipman, P. Schraml, M. Colombi, G. Raefle, P. Dalquen and C.U. Ludwig (1993). p53 mutations in human, primary non-small cell lung carcinoma. C.R. Brupbacher Foundation First Scientific Symposium: p53 in Growth Control and Neoplasia. Zurich, CH.

10. R. Shipman, P. Schraml, M. Colombi, and C.U. Ludwig (1994). Allelic loss and alteration of tumour suppressor genes in human lung and bladder carcinoma. 10th Annual Meeting of the OAO/GTOR (Upper Rhine Oncology Association). Basel, CH.

11. R. Shipman and C.U. Ludwig (1994). Allelic deletion, mutation and expression of putative tumour suppressor genes in human non-small cell lung carcinoma. Keystone Symposia on Molecular and Cellular Biology: Molecular Basis of Cancer Therapy.

Tamarron, CO.

12. R. Shipman, P. Schraml, M. Colombi, and C.U. Ludwig (1994). Alterations of putative tumour suppressor genes in human non-small cell lung carcinoma (NSCLC). 26th Annual Meeting of the USGEB/USSBE (Swiss Union of Biological Sciences). Bern, CH.

13. R. Shipman, P. Schraml and C.U. Ludwig (1994). Preferential allelic loss of the catalase gene (CAT) at 11p13 in human non-small cell lung cancer. Swiss Society for Oncology, Bern, CH.

14. P. Schraml, R. Shipman and C.U. Ludwig (1994). Differentially expressed genes in normal lung and non-small cell lung cancer. Swiss Society for Oncology. Bern, CH.

15. R. Shipman, P. Schraml, and C.U. Ludwig (1995). Preferential allelic loss of catalase and alterations to the p53 and WT1 genes in primary non-small cell lung cancer. 86th Annual Meeting of the AACR. Toronto, ON.

16. Shipman, R., P. Schraml, and C.U. Ludwig (1995). Preferential allelic loss of the CAT locus at chromosome 11p13 and the isolation of genes involved in the development of non-small cell lung cancer. C.R. Brupbacher Foundation Second Scientific Symposium: Genetic Predisposition to Cancer. Zurich, CH.

17. P. Schraml, R. Shipman and C.U. Ludwig (1995). Identification and characterisation of genes down-regulated in non-small cell lung cancer. C.R. Brupbacher Foundation Second Scientific Symposium: Genetic Predisposition to Cancer. Zurich, CH.

18. M.E. Saunders and R. Shipman (1997). Complete p53 gene analysis using the OpenGene system: Mutation detection in genomic DNA from archival and fresh clinical specimens. 3rd Annual Meeting of the Association for Molecular Pathology, San Diego, CA.

19. R. Shipman and M.E. Saunders (1998). Complete p53 gene analysis using the OpenGene system: Mutation detection in genomic DNA from archival and fresh clinical specimens.
American Association for Cancer Research Annual Meeting, New Orleans, LA.

20. M.E. Saunders, R. Shipman and R.C.K. Jordan (1998). Complete p53 gene analysis in head and neck cancer: Mutation detection in genomic DNA from archival specimens. American Association for Cancer Research Annual Meeting, New Orleans, LA.

21. R. Shipman and M.E. Saunders (1998). Complete p53 gene analysis using the OpenGene system: Mutation detection in genomic DNA from archival and fresh clinical specimens. 4th Annual Meeting of the Association for Molecular Pathology, Crystal City, VA.

22. R. Shipman and M.E. Saunders (1998). Complete p53 gene analysis using the OpenGene system: Mutation detection in genomic DNA from archival and fresh clinical specimens. 48th Annual Meeting of the American Society for Human Genetics, Denver, CO.

23. M.E. Saunders, R. MacKenzie, R. Shipman, E. Fransen, R. Gilbert and R.C.K. Jordan (1998). Full-length p53 gene sequencing in head and neck cancer and outcome radiation therapy. 22nd Annual Meeting of the Eastern Great Lakes Head and Neck Association, Toronto, ON.

24. R. Shipman (1999). Complete p53 mutation analysis, allelic loss and microsatellite instability in non-small cell lung cancer. American Association for Cancer Research Annual Meeting, Philadelphia, PA.

25. M.E. Saunders, R. MacKenzie, R. Shipman, E. Fransen, R. Gilbert and R.C.K. Jordan (1999). Full-length p53 gene sequencing in head and neck cancer and outcome radiation therapy. American Association for Cancer Research Annual Meeting, Philadelphia, PA.

26. D. Nuesca, S. Jacob, F. Jamieson, G. Broukhanski and R. Shipman (1999). Rapid detection of antibiotic resistance-associated mutations in 10 gene targets in Mycobacterium tuberculosis using the OpenGene system. 99th General Meeting of the American Society for Microbiology, Chicago, IL.

27. R. Shipman (1999).Complete p53 mutation analysis, allelic loss and microsatellite instability in non-small cell lung cancer. 50th Annual Meeting of the Canadian Association of Pathologists, Calgary, AB.

28. D. Nuesca, S. Jacob, F. Jamieson, G. Broukhanski and R. Shipman (1999). Rapid detection of antibiotic resistance-associated mutations in 12 gene targets in Mycobacterium tuberculosis using the OpenGene system. 50th Annual Meeting of the Canadian Association of Pathologists, Calgary, AB.

29. M.E. Saunders, R. MacKenzie, R. Shipman, E. Fransen, R. Gilbert and R.C.K. Jordan (1999). Full-length p53 gene sequencing in head and neck cancer and outcome radiation therapy. 50th Annual Meeting of the Canadian Association of Pathologists, Calgary, AB.

30. R. Shipman, S. Carmichael, S. Fung and T. Ewart (2001). The Affect of Hybridization Conditions on Fluorescent Signal Intensities Recovered from Microarrays. 7th Annual Meeting of the Society for Biomolecular Screening, Baltimore, MD.

31. R. Shipman, S. Fung, A. Tang, S. Carmichael and T. Ewart (2003). APTarray: An Acquired Pathogen Titre Array for the Determination of Serum Antibody Levels. 9th Annual Meeting of the Society for Biomolecular Screening, Portland, OR.

32. R. Shipman, E. Rose, K. Marseu, J. Sidhu and D.K.H Lee (2005). Gene Expression Analysis of Drug Treated Cell Lines using a Human ABC Transporter Microarray. AAPS

Workshop on Drug Transporters in ADME: From the Bench to the Bedside. Parsippany, NJ.

33. R. Shipman, E. Rose, K. Marseu, J. Sidhu and D.K.H Lee (2005). Gene Expression Profiling using a Human ABC Transporter Microarray. American Association for Cancer Research Annual Meeting, Anaheim, CA.

34. R. Shipman, E. Rose, K. Marseu, J. Sidhu and D.K.H Lee (2005). A Microarray for ABC Transporter Gene Expression Profiling. Cambridge Healthtech Institute Microarrays in Medicine. Boston, MA.

35. J. Morrison, J. Sidhu, D.K.H. Lee and R. Shipman (2006). DTEx™ - Gene Expression Profiling using a Human ABC Transporter Microarray. World Microarray Congress. Vancouver, BC.

36. R. Shipman, J. Morrison, J. Sidhu and D.K.H. Lee (2007). Time Course Analysis of Drug Transporter, Cytochrome P450 and Nuclear Receptor Gene Expression Profiles in 21 Day Caco-2 Cell Cultures. AAPS Workshop on Drug Transporters in ADME: From the Bench to the Bedside. North Bethesda, MD.

37. J. Morrison, J. Sidhu, D.K.H. Lee and R. Shipman (2007). Analysis of Drug Transporter, Cytochrome P450 and Nuclear Receptor Gene Expression Profiles in Human Hepatocytes. AAPS Workshop on Drug Transporters in ADME: From the Bench to the Bedside. North Bethesda, MD.

38. R. Shipman, J. Morrison, J. Sidhu and D.K.H. Lee (2007). Expression Profiling of Drug Transporter, Cytochrome P450 and Nuclear Receptor Genes in Caco-2 Cells using DTEx™ Microarrays. DDI-2007, 10th International Conference on Drug-Drug Interactions: Scientific and Regulatory Updates and DDI Technologies in Depth: Enzyme Inhibition, Enzyme Induction and Drug Transporter Interactions. Institute for Scientific Exchange. Bellevue, WA

VIII. Operating Grants and Fellowships:

1981 B.C. Cancer Foundation Studentship.

1982 Graduate Student Research Assistantship.

1983 University Graduate Student Fellowship.

1984 University Graduate Student Fellowship.

1991 Grant #31-30098.90 (SFr 215,819).
Deletions and mutations of putative tumour suppressor genes in human non-small cell lung cancer. Swiss National Research Fund (Schweizerischer Nationalfonds zur

Foerderung
der wissenschaftlichen Forschung).

1992 Grant #AKT 318 (SFr. 40,000).
Cloning of putative tumor suppressor genes by subtraction hybridisation of normal lung tissue cDNA versus lung carcinoma cDNA of the same patient. Cancer Research Switzerland (Krebsforschung Schweiz).

1993 Grant #31-36494.92 (SFr 345,000).
Isolation of genes from chromosome 11p13, that are deleted in human non-small cell lung cancer, using a yeast artificial chromosome-based approach. Swiss National Research Fund (Schweizerischer Nationalfonds zur Foerderung der wissenschaftlichen Forschung).

1993 Grant # FOR 396 (SFr 160,000).
Characterisation of cDNAs expressed in normal human lung tissue and not in primary non-small cell lung carcinoma (NSCLC). Swiss Cancer League (Schweizerische Krebsliga).

IX. Teaching experience:

1982, Teaching assistant and Lab instructor. Undergraduate Microbiology Courses, Department of Microbiology, UBC, Vancouver, BC, Canada.

1983, Teaching assistant and Lab instructor. Undergraduate Microbiology Courses, Department of Microbiology, UBC, Vancouver, BC, Canada.

1984, Teaching assistant and Lab instructor. Undergraduate Microbiology Courses, Department of Microbiology, UBC, Vancouver, BC, Canada.

1994, Course instructor. PCR course for clinical researchers (May 19-20), Boehringer Mannheim AG (Switzerland), Laborschule ZLF, Kantonsspital Basel, Basel, Switzerland.

1995, Course instructor. PCR "trouble-shooting" Workshop (March 9-10), Boehringer Mannheim AG (Switzerland), Laborschule ZLF, Kantonsspital Basel, Basel, Switzerland.

EXHIBIT B

1. – 48. (Previously Cancelled)

49. (Currently Amended) An array comprising two or more nucleic acid molecules immobilized on a substrate, wherein at least two of the nucleic acid molecules have a nucleic acid sequence consisting of ~~the nucleic acid sequence as shown in~~ SEQ ID ~~NOS~~ NO:12, 15, 21, 22, 23, 24, 25, 26, 35 or 44.

50. (Previously Amended) The array according to claim 49, wherein the array is a microarray.

51 – 77. (Previously Cancelled)

78. (Previously Amended) An array for screening a sample for the presence of nucleic acid molecules that encode human ABC transporters, the array comprising a substrate having immobilized in distinct spots thereon at least 10 nucleic acid probes, wherein 10 of the probes consist of:

1) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter B1, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 12;
2) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter B4, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 15;
3) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter B11, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 21;

4) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter C1, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 22;

5) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter C2, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 23;

6) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter C3, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 24;

7) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter C4, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 25;

8) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter C5, wherein the nucleotide sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 26;

9) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter D1, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 35; and

10) a probe that specifically hybridizes to a nucleic acid sequence encoding human ABC transporter G2, wherein the nucleic acid sequence of the probe is a nucleic acid sequence consisting of SEQ ID NO. 44.

79. – 85. (Previously Cancelled)